CONDUCTOMETRIC STUDIES OF BULK AND NANO-COPPER SULFATE WITH SPIRAMYCIN ADIPATE (SA) IN MIXED SOLVENTS (MeOH-H₂O) AT 298.15K.

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ABSTRACT

On using conductometric technique, the specific conductivities ($K_s$) of bulk and nano-CuSO₄ solutions were measured in the range of mixed solvent (MeOH-H₂O) at 298.15 K in the absence and in the presence of Spiramycin adipate (SA) antibiotic. From the experimental data, the molar conductance ($\Lambda_m$), the limiting molar conductance ($\Lambda_0$), the association constant ($K_A$) and Gibbs free energy change ($\Delta G_A$) were calculated by using Fuoss-Shedlovsky and Fouss-Kraus extrapolation methods. The interaction of Spiramycin adipate with bulk and nano-CuSO₄ in mixed solvent (MeOH-H₂O) has been found to form two complexes 1:1 and 1:2 (metal to ligand molar ratio).

Key words: Spiramycin adipate, nanotechnology, association constant, Fouss-Kraus extrapolation.

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INTRODUCTION

Nanotechnology is viewed as a developing technology because of the likelihood to advance well-established products and to make new products with totally new aspects and functions with tremendous potential in an extensive variety of applications. Nanoparticles have broad variety of applications in biomedicine field such as to deliver pharmaceutics, for diagnostic approaches and in addition for the therapeutic purposes. This is due to the large surface to volume proportion of nanoparticles compared with bulk particles. Nano materials, a new branch of materials research, are attracting a great deal of attention because of their potential applications in areas such as optoelectronics (OE) [1], catalysis [2], single-electron transistors and light emitters [3] and biological applications. Copper (II) ions (Cu\(^{2+}\)) are readily soluble in water, where they function at low concentration as bacteriostatic substances, fungicides, and wood preservatives [4]. Recently, copper (II) sulfate has been used as a Lewis acid catalyst for various organic transformations [5, 6]. It is an inexpensive, available and extremely safe reagent to be used in chemical reactions such as catalytic reactions [7]. The choice of copper in the present research is attributed to copper (II) ions are reported to have antimicrobial activity against a number of species of bacteria and fungi [8]. Spiramycin adipate (SA) is a macrolide antimicrobial agent with activity against gram- positive organisms, including Streptococcus pyogenes (group A beta- hemolytic streptococci), S. Viridans, and Corynebacterium Diphtheria. Spiramycin also has activity against some gram- negative bacteria such as Neisseria meningitidis, Bordetella pertussis, and Campylobacter. Spiramycin adipate (SA) is used in pregnant women to decrease the risk of toxoplasmosis transmission to the fetus [9]. The complexation of Spiramycin adipate (SA) antibiotic with bulk and nano metal salts have a wide variety of applications in medicinal and analytical chemistry and also expand the broad spectrum against various infections.

Conductivity estimations are utilized routinely as a part of numerous applications as a fast, economical and reliable way of measuring the ionic species in any solution [10], inexpensive way of determining the ionic strength of a solution. The conductivity studies also provide information about complexation interactions such as association constant and Gibbs free energy change and other parameters show the differential manner between bulk and nano metal salts.

In the present work, we are studying the conductivity of bulk and nano- CuSO\(_4\) in absence and presence of ligand (Spiramycin adipate antibiotic) using different molar ratios of (MeOH-H\(_2\)O) mixed solvent at 298.15 K by applying Fuoss-Shedlovsky, Fouss-Kraus extrapolations, we were able to evaluate the values of \((\Lambda_0)\), \((K_A)\) \((\Delta G_A)\)and to make an acceptable discussion.
EXPERIMENT

A. Materials and solvent

Spiramycin adipate (SA) was supplied from Atco. Pharma as white solid, the structure is shown in scheme 1 and copper sulfate pentahydrate from Merk Germany, Methanol from El Nasr Pharmaceutical Chemicals Co. and used directly without purification; double- distilled water was used throughout this study.

![Scheme 1. The structure of Spiramycin adipate antibiotic](image)

B. Apparatus

The specific conductance values were recorded using conductivity bridge HANNA, H1 8819N with a cell constant equal 1cm⁻¹. The conductometer was connected to the type Kottermann 4130 ultra-thermostat. In a typical experiment, 20 mL of Spiramycin adipate (SA) solution (1x 10⁻⁴M) was placed in the titration cell, thermostated at the present temperature and the conductance of the solution was measured after the solution reached thermal equilibrium. Then, a known amount of CuSO₄. 5H₂O solution (1x 10⁻³M) was added in a stepwise manner using a calibrated micropipette.

C. Preparation of nano- copper sulfate

Nano- copper sulfate pentahydrate was prepared by shaking it in ball-mill apparatus of type Retsch MM2000 swing mill for period of one hour. The mill has 10 cm³ stainless steel tubes. Two stain steel balls of 12 mm diameter were used. Ball milling was performed at 20225 Hz at room temperature and investigated under transmission electron microscopy (TEM).
Result and discussion

A. TEM image for nano-copper sulfate penthydrate.

The picture of nano-CuSO$_4$.5H$_2$O from transmission electron microscope (TEM) is represented in Fig. 1 from an image we can deduce that nano-CuSO$_4$.5H$_2$O is either in the form of irregular spheres or deformed spheres, the images show also crystalline form and the dimensions of the particles ranging from 20 to 40 nm.

Fig. 1 TEM image of nano-CuSO$_4$.5H$_2$O

B. Association thermodynamic parameters of the bulk and nano-copper sulfate alone in different percentage of mixed solvent (MeOH-H$_2$O) at 298.15 K.

The specific conductance values (K$_s$) of different concentrations of bulk and nano-CuSO$_4$ in MeOH-H$_2$O mixtures in the absence of Spiramycin adipate (SA), were measured experimentally and from which the values of molar conductance (Λ$_m$) were calculated [11] by using eq. (1):

$$\Lambda_m = \frac{(K_s - K_{solv})K_{cell} \times 1000}{C}$$  \hspace{1cm} (1)

Where (K$_s$) and (K$_{solv}$) are the specific conductance of the solution and the solvent, respectively; (K$_{cell}$) is the cell constant and (C) is the molar concentration of CuSO$_4$.

The concentration dependence of the molar conductance were studied by plotting the relation between the (Λ$_m$) and (C$^{1/2}$) for bulk and nano-CuSO$_4$ in absence of Spiramycin adipate (SA) antibiotic as shown in Fig 2. The data obtained are represented in Table 1.
0.0030 0.0035 0.0040 0.0045 0.0050 0.0055 0.0060 0.0065

0
500
1000
1500
2000
2500

Molar conductance /m (S. cm\(^2\).mol\(^{-1}\))

C

\(C^{1/2}\)

20 % MeOH
40 % MeOH
60 % MeOH

at 298.15 K

\(\Lambda_m\) vs. \(C^{1/2}\) for bulk CuSO\(_4\) at 298.15 K

\(\Lambda_m\) vs. \(C^{1/2}\) for nano-CuSO\(_4\) at 298.15 K

Fig. 2. The relation between molar conductance (\(\Lambda_m\)) and \(C^{1/2}\) of nano CuSO\(_4\) in mixed solvent (MeOH-H\(_2\)O) at 298.15 K.

Table 1. Limiting molar conductance (\(\Lambda_o\)), association constant (K\(_A\)) and Gibbs free energy change (\(\Delta G_A\)) for bulk and nano-CuSO\(_4\) in (MeOH-Water) mixtures at 298.15 K.

<table>
<thead>
<tr>
<th>Vol % of MeOH</th>
<th>Bulk CuSO(_4) at 298.15 K</th>
<th>Nano-CuSO(_4) at 298.15 K</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\Lambda_m)</td>
<td>(\Lambda_o)</td>
</tr>
<tr>
<td>20</td>
<td>666.15</td>
<td>4268.94</td>
</tr>
<tr>
<td>40</td>
<td>367.19</td>
<td>2229.78</td>
</tr>
<tr>
<td>60</td>
<td>231.77</td>
<td>1599.49</td>
</tr>
</tbody>
</table>

\(\Lambda_o\) in (S cm\(^2\).mol\(^{-1}\)), \(\Lambda_m\) in (S cm\(^2\).mol\(^{-1}\)) and \(\Delta G_A\) in (kJ mol\(^{-1}\)).

It is clear that the molar conductance values (\(\Lambda_m\)) decrease linearly by increasing both of metal concentration and the percentages of MeOH. We found that the molar conductance (\(\Lambda_m\)) for all solutions under study (in the used aqueous–organic mixed solvents) decreases with increase in ionic concentration. Limiting molar conductance (\(\Lambda_o\)) of the salt under investigation is inversely related to the fraction of the organic–aqueous solvents at the same temperature as the following direction (20%<10%). This behavior may be due to the formation of hydrogen bond which leads to the interaction of alcohol and H\(_2\)O molecules, and so reduce the ions mobility and decrease the \(\Lambda_o\) values with higher fractions of the non-aqueous solvent [12].

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C. Association thermodynamic parameters of the bulk and nano- copper sulfate in the presence of Spiramycin adipate in mixed solvent (MeOH-H$_2$O) at 298.15 K.

The limiting molar conductance ($\Lambda_0$) at infinite dilutions were estimated for bulk and nano metal salts in mixed solvent at different temperatures in the presence of ligand by plotting the relation between ($\Lambda_m$) and molar ratio [M]/[L] as appeared in Fig. 3 obtained on a straight lines with sharp breaks at definite metal concentrations, representing stoichiometric ratios (L: M) in all the mixed solvent.

The experimental data of ($\Lambda_m$) and ($\Lambda_0$) were analyzed by using Fuoss-Shedlovesky extrapolation method [13, 21] to estimate ($K_A$) of bulk and nano metal salts in the presence of ligand. The above mentioned method is given by the sequence of the equations from (2) to (9).

\[
\frac{1}{\Lambda_m S(z)} = \frac{1}{\Lambda_0} + \left( \frac{K_A}{\Lambda_0^2} \right) (CA_m \gamma_\pm^2 S(z)) \\
S(z) = \left[ \frac{z}{2} \left( 1 + \left( \frac{z}{2} \right)^2 \right)^{1/2} \right]^2 \\
z = \frac{S(\Lambda_m C)^{1/2}}{\Lambda_0^{3/2}} \\
S = a\Lambda_0 + b \\
a = \frac{8.2 \times 10^5}{(\varepsilon T)^{1/2}} \\
b = \frac{0.825}{\eta_0 (\varepsilon T)^{1/2}} \\
\log \gamma_\pm = -A(\alpha C)^{1/2} \left[ 1 + Br^0 (\alpha C)^{1/2} \right] \\
\alpha = \frac{\Lambda_m S(z)}{\Lambda_0}
\]

Where $K_A$ is association constant, C is the Molar concentration of metal salts, $\gamma_\pm$ is the activity coefficient, S ($z$) is the Onsager constant, $\alpha$ is the degree of dissociation, T is the absolute temperature, (A) and (B) are the Debye - Hückel constants, ($r^0$) is the ion size parameter, ($\eta_0$) and ($\eta$) are the viscosity and the dielectric constants of the mixed solvent used respectively.

On using Eq. (2) and from the linear plot of $1/\Lambda_m S(z)$ vs. $C \Lambda_m \gamma_\pm^2 S(z)$, (Fuoss-Kraus method) [22, 23] ($K_A$) values could be evaluated, where the slope equal to $K_A/\Lambda_0^2$ and the intercept equals $1/\Lambda_0$ are given in Fig 4, 5.
Fig. 3. Molar conductance ($\Lambda_m$) against the molar ratio $[M]/[L]$ for bulk and nano- CuSO$_4$ to Spiramycin adipate in mixed solvent (MeOH-H$_2$O) at 298.15 K.

On drawing the relation between molar conductance ($\Lambda_m$) and concentration of metal ions (Cu$^{2+}$) and ligand (Spiramycin adipate) ($M/L$) curvatures obtained with two inflections at 1:1 and 1:2 molar ratios. The association parameters for two stoichiometric complexes obtained 1:1 and 1:2 ($M/L$) from the interaction of bulk and nano CuSO$_4$ with ligand (Spiramycin adipate) were evaluated from Fig. 4, 5 and by applying Fuoss- Kraus method. The data were given in Tables 2, 3.
Stoichiometric ratio (L:M) of (1:1) at 298.15 K  
Stoichiometric ratio (L:M) of (1:2) at 298.15 K

Fig. 4. Fuoss-Kraus plot for bulk CuSO₄ in presence of Spiramycin adipate of 1:1 and 1:2 (L: M) complex in (MeOH-H₂O) mixtures at 298.15 K.
Stoichiometric ratio (L:M) of (1:1) at 298.15 K  
Stoichiometric ratio (L:M) of (1:2) at 298.15 K

**Fig. 5.** Fuoss-Kraus plot for nano-CuSO₄ in presence of Spiramycin adipate of 1:1 and 1:2 (L:M) complex in (MeOH-H₂O) mixtures at 298.15 K.

The evaluation of Gibbs free energies of association (ΔGₐ) and the transfer Gibbs free energies of association (ΔGₜ) (for (1:1) and (1:2) complexes of bulk and nano-CuSO₄ with Spiramycin adipate (SA) antibiotic in (MeOH-H₂O) mixtures, at 298.15 K were gained according to eq. (10, 11) [24-32]. All the parameters calculated are given in Table 2.

$$\Delta G_a = -RT \ln K_A$$  \hspace{1cm} (10)
$$\Delta G_t = \Delta G_A (s) - \Delta G_A (H_2O)$$  

(11)

**Table 2.** The values of limiting molar conductance, association constant and Gibbs free energy change for bulk CuSO₄ in presence of Spiramycin adipate in (MeOH-H₂O) mixtures at 298.15 K.

<table>
<thead>
<tr>
<th>Vol % of MeOH</th>
<th>[M]:[L]</th>
<th>C₁/² x 10⁻³</th>
<th>Λₘ</th>
<th>Λ₀</th>
<th>γ₂</th>
<th>S(Z)</th>
<th>Kₐ x 10⁵</th>
<th>ΔGₐ</th>
<th>ΔGₜ</th>
<th>ΔGₘ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1:2</td>
<td>6.90</td>
<td>541.597</td>
<td>1051.99</td>
<td>0.9748</td>
<td>1.002</td>
<td>15.59</td>
<td>-35.35</td>
<td>-26.081</td>
<td>-9.269</td>
</tr>
<tr>
<td>40</td>
<td>1:1</td>
<td>9.53</td>
<td>185.919</td>
<td>300.849</td>
<td>0.9571</td>
<td>1.004</td>
<td>1.90</td>
<td>-30.13</td>
<td>-20.861</td>
<td>-9.269</td>
</tr>
<tr>
<td></td>
<td>1:2</td>
<td>6.90</td>
<td>308.824</td>
<td>553.928</td>
<td>0.9704</td>
<td>1.002</td>
<td>5.48</td>
<td>-32.76</td>
<td>-23.491</td>
<td>-9.269</td>
</tr>
<tr>
<td>60</td>
<td>1:1</td>
<td>9.53</td>
<td>110.121</td>
<td>185.145</td>
<td>0.9496</td>
<td>1.006</td>
<td>1.45</td>
<td>-29.46</td>
<td>-20.191</td>
<td>-9.269</td>
</tr>
<tr>
<td></td>
<td>1:2</td>
<td>6.90</td>
<td>189.496</td>
<td>365.916</td>
<td>0.9657</td>
<td>1.003</td>
<td>35.37</td>
<td>-37.39</td>
<td>-28.121</td>
<td>-9.269</td>
</tr>
</tbody>
</table>

Λ₀ in (S cm².mol⁻¹), Λₘ in (S cm².mol⁻¹) and ΔGₐ in (kJ mol⁻¹).

**Table 3.** The values of limiting molar conductance, association constant and Gibbs free energy change for nanoCuSO₄ in presence of Spiramycin adipate in (MeOH-H₂O) mixtures at 298.15 K.

<table>
<thead>
<tr>
<th>Vol % of MeOH</th>
<th>[M]:[L]</th>
<th>C₁/² x 10⁻³</th>
<th>Λₘ</th>
<th>Λ₀</th>
<th>γ₂</th>
<th>S(Z)</th>
<th>Kₐ x 10⁵</th>
<th>ΔGₐ</th>
<th>ΔGₜ</th>
<th>ΔGₘ</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>1:1</td>
<td>9.53</td>
<td>193.399</td>
<td>316.127</td>
<td>0.9622</td>
<td>1.003</td>
<td>0.34</td>
<td>-25.87</td>
<td>-16.601</td>
<td>-9.269</td>
</tr>
<tr>
<td></td>
<td>1:2</td>
<td>6.90</td>
<td>298.739</td>
<td>504.097</td>
<td>0.9729</td>
<td>1.002</td>
<td>2.18</td>
<td>-30.47</td>
<td>-21.201</td>
<td>-9.269</td>
</tr>
<tr>
<td>40</td>
<td>1:1</td>
<td>9.53</td>
<td>120.352</td>
<td>162.509</td>
<td>0.9531</td>
<td>1.006</td>
<td>0.32</td>
<td>-25.718</td>
<td>-16.449</td>
<td>-9.269</td>
</tr>
<tr>
<td></td>
<td>1:2</td>
<td>6.90</td>
<td>167.227</td>
<td>258.791</td>
<td>0.9681</td>
<td>1.003</td>
<td>1.26</td>
<td>-29.603</td>
<td>-20.334</td>
<td>-9.269</td>
</tr>
<tr>
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<td>1:1</td>
<td>9.53</td>
<td>106.161</td>
<td>164.636</td>
<td>0.9476</td>
<td>1.006</td>
<td>1.56</td>
<td>-29.645</td>
<td>-20.376</td>
<td>-9.269</td>
</tr>
<tr>
<td></td>
<td>1:2</td>
<td>6.90</td>
<td>172.899</td>
<td>314.139</td>
<td>0.9647</td>
<td>1.003</td>
<td>4.52</td>
<td>-32.283</td>
<td>-23.014</td>
<td>-9.269</td>
</tr>
</tbody>
</table>

Λ₀ in (S cm².mol⁻¹), Λₘ in (S cm².mol⁻¹) and ΔGₐ in (kJ mol⁻¹).

**CONCLUSION**

We concluded from this work that the complex association parameters are greater for 1:2 (M/L) stoichiometry complexes than that of 1:1 (M/L) stoichiometry complexes for both bulk copper sulfate and nano copper sulfate in all used mixed solvents at 298.15 K indicating that more possibility to occur and observed from given data that the maximum complexation between bulk and nano- copper ions and spiramycin adipate antibiotic were by using 60% MeOH in the mixtures. Whereas the least complexing ability at 40% by volume of MeOH.

**REFERENCES**


